Single Molecule DNA Sequencing with Inelastic Tunneling Spectroscopy STM

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There is heightened interest in sequencing a genome, which is essential to personalized medicine. The inelastic electron tunneling spectroscopy is a well-established and powerful tool that allows the measurement of the characteristic energies of local and extended modes. The inelastic tunneling spectroscopy scanning tunneling microscopy (IETS-STM) serves to measure the local electronic properties coupled to local vibrational modes of atoms or molecules on a surface. Here we propose the use of STM to sequence a single DNA molecule.

The setup we propose, as shown in Fig. 1, is to use STM in a two-step process. First, we propose to locally excite the vibrational modes by injecting energetic electrons through the molecule into the substrate. The energy of the injected electrons is transferred to excite the vibration of individual base pairs. Second, to measure the local density of states (LDOS) in the vicinity of the injection point. The LDOS at a finite bias but with much smaller drive currents will allow measurement of the inelastic processes revealing the existence of the local vibrational modes. The features in LDOS once the local modes are excited are of main interest.

To illustrate how this technique works, we use the Peyrard-Bishop-Holstein model to describe the surface conduction electrons coupled to the lattice dynamics degrees of freedom in the single DNA molecule. Within the Peyrard-Bishop (PB) model for the displacement field, the most relevant degrees of freedom, namely the *transverse* stretching of the hydrogen bonds connecting complementary bases in the opposite strands of the double helix, are captured. The PB with fitted model parameters has been successfully compared with the denaturation experiments on short homogeneous sequence. A key observation here is that the adenine-thymine (A-T) base pair has two hydrogen bonds, while the guanine-cytosine (C-G) base pair has three hydrogen bonds. This difference leads to very different energy of low-lying vibrational excitations, which will be reflected in the lost tunneling electron energy to excite these modes, as will be shown below.

We have used the Green's function technique to calculate the change in the LDOS of electrons on the substrate. The correlation function for the displacement field of the base pair, which is involved in the electron self-energy is solved fully quantum mechanically via exact diagonalization. The derivative of the LDOS correction at the individual base pair, which corresponds to d^2I/dV^2 measured in the IETS experiment, is displayed in Fig. 2. The peaks in the figure identify the first excitation energy of the quantum oscillator corresponding to the A-T and C-G base pairs. They are $E = 4.703$ meV and $E = 9.259$ meV for A-T and C-G base pairs, respectively. The second group of peaks with much weaker intensity, which corresponds to the second low-lying excitations, comes uniquely from the anharmonicity of the base-pair potential. This feature is absent for the case of a harmonic potential.

Fig. 1. Proposed experimental realizations: A single DNA molecule is placed on the metallic surface. An STM is used to inject/extract electrons from the substrate. Electron-vibration mode coupling can excite the local modes on the molecule.

STM tip

Electronic states in substrate

Single DNA molecule
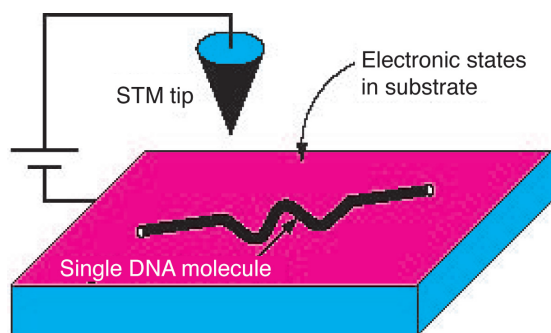
Once the different characteristic energies of the vibrational modes associated with A-T and C-G bases are known, one is able to map out the spatial dependence of the energy-derivative LDOS. The quantity is mapped out through the imaging measurement of d^2I/dV^2 in an STM experiment. To be specific, we consider the following sequence as an example:

A C T C C A A
| | | | | | |
T G A G G T T

Figure 3 shows the spatial variation of the energy derivative of the LDOS correction. The strongest intensity registers the location of individual A-T and C-G base pairs. The ripples away from the brightest spots simply manifest the Friedel oscillation. Our calculations suggest using a metallic substrate with high Fermi wave vector to achieve a high spatial resolution.

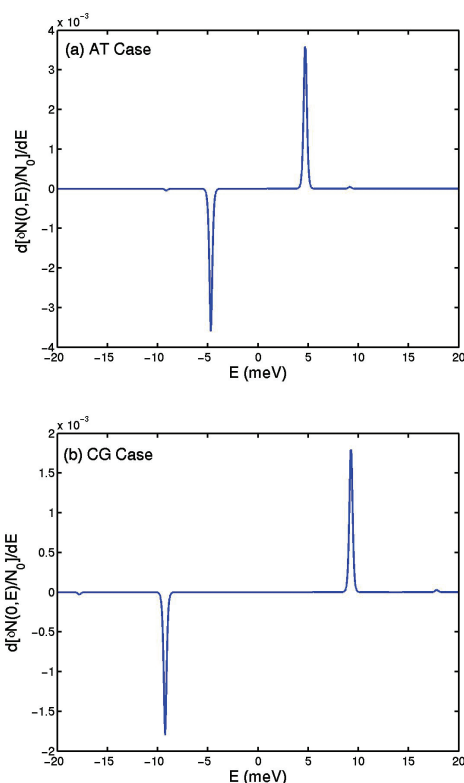*For more information contact Jian-Xin Zhu at jxzhu@lanl.gov.*

Fig. 2.
The derivative of the correction to the local density of states calculated at the location of an individual base pairs as a function of energy at low temperatures.
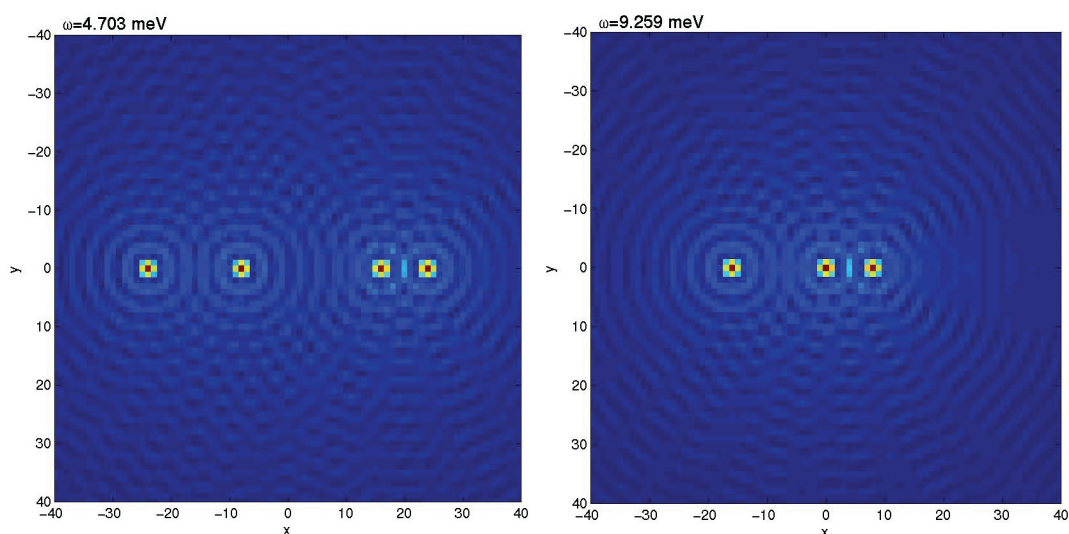
Fig. 3.
The spatial image of the derivative of the LDOS correction at energy ω = 4.703 meV and 9.259 meV at low temperatures.